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CHORIO-EPITHELIOMA MALIGNUM.

BY

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University of Vermont; Gynæcologist to the Montreal General Hospital
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My excuses for bringing this subject before you are first: my having been so fortunate as to have had under my care at the Montreal General Hospital, a second patient afflicted with this dread disease, which is interesting so many investigators all over the world, and, second, my having been able to collect histories of seven cases which have been observed in Canada.

As the officer in command of an army sends out his spies, engineers and sappers to observe and prepare the country to be invaded, so does the impregnated ovum send forth its advance guard of cells which burrow beneath the uterine mucosa and prepare a resting place where it may remain secure during its further development. These trophoblastic cells ordinarily disappear after having performed their normal function, but in a few cases, owing to some unexplained cause, they give rise to a growth, which, in the vast majority of cases, ultimately ends by depriving of life the organism which has sustained and nourished it, and which, therefore, has been spoken of by Pinto¹ as "a sustained decidual reaction."

This growth was first described in 1888, by Sängér,² who considered it to be a sarcoma derived from the decidua, for which reason he called it "Deciduoma Malignum." In 1895, Marchand questioned the correctness of this view, holding that it did not arise from the decidua alone, but from the epithelium of the syncytium and Langhan's layer, that is to say, from the lining of the villi, thus suggesting a double origin, viz: a foetal from Langhan's layer and a maternal from the syncytium. Later, however, in 1895, he modified this theory, believing that the syncytium did not arise from the maternal tissues, but from the foetal ectoderm, and this theory, viz: that the disease is entirely of foetal origin, is that which is held at present.

Schmauch³ claims that the vitality of the trophoblast is limited to the formation of but three varieties of cells, viz: the cells of Langhan's

layer, the plasmodium or syncytium, and the syncytial cells. He says that "it is the surroundings which give chorio-epitheliomatous cell its form. It is neither an epithelial nor connective tissue cell, it is something between these two. Consequently, it is able to assume the characteristics of both."⁴ These cells being present in all pregnancies, what determines their malignancy? This is a difficult question to answer, but probably there is some change in the maternal organism which renders it less able to offer an effectual resistance to their undue proliferation. The possibility of this loss of inhibitory power being due to an alteration in the blood serum is a question of importance and well worth working out. It is not simply due to a transplantation of epithelium, as such a proceeding is followed by a proliferation of the cells which is but temporary, this fact lending strength to the theory of a change in the maternal structures being the cause of the malignancy. Neither the deportation of the villi nor the proliferation of the epithelium proves the malignancy of the growth. The former occurs in all pregnancies, and the epithelium is innocuous as long as it remains attached to the villus and does not penetrate the surrounding tissues. Kröner⁵ suggests that possibly deep implantation of the ovum may favour the development of chorio-epithelium, but against this may be urged the fact that in all uteri with adherent placenta the villi will be found to have burrowed deeply into the muscular tissue without any intervening decidual tissue. In this instance, Veit speaks of these villi as being "deported," but this application of the term is misleading, as they remain attached to their source of origin and the metastases are due to an actual deportation or migration of portions of villi or masses of cells to more or less distant parts by the bloodstream.

Etiology.—Pregnancy is the great predisposing factor in the causation of chorio-epithelioma, and, therefore, it is more prevalent during the period of woman's greatest sexual activity than at any other age. The average age in Teacher's⁶ list was 35, with slight rises at either extremity due to the tendency of immature or old uteri to produce abortions, especially hydatid moles. In my own list of 227 cases published in 1905,⁷ the age was not stated in 19. Four were under 20, 105 were between 20 and 30, 80 between 31 and 40, 57 between 41 and 50, and 12 over 50 years of age. While pregnancy precedes the great majority of cases, it is not an essential factor, the disease having been observed in young girls before the onset of menstruation, in women well past the menopause, and even in the male. Bostrom⁸ saw a man aged 32 years who was operated on for cerebral tumour which the microscope showed to contain decidual masses and the autopsy revealed metastases in the lungs

and on the peritoneum, all of which contained chorio-epitheliomatous tissue. Ritchie performed an autopsy on a man in whose mediastinum were two masses, one of which was a dermoid and the other a tumour composed of cells similar to those seen in the disease under discussion. Two of our own confreres, Drs. Keenan and Garrow, have at present a patient from whom a diseased testicle was removed, and who had cutaneous metastases composed of true chorio-epithelial tissue. Those cases in which the disease does not follow pregnancy, are probably due to one of two causes. Either it arises from teratomata or there has been inclusion by the developing ovum of some trophoblastic cells which have lain dormant until some mysterious, undetermined agency has caused their active proliferation.

Hydatid degeneration of the chorion has an undoubted influence in predisposing patients to this malady. In my own series, the nature of the pregnancy was stated in 262 cases; 36.78 per cent. were seen to follow molar pregnancies; 31.80 per cent. followed abortions, and 26.43 per cent. occurred after full term labours. Gebhardt states that one pregnancy in every 728 is terminated by the formation of a mole, while Williams gives a much lower ratio, viz: 1-2400. Berry Hart claims that only one mole in every thousand becomes malignant, which is not a very high rate of malignancy.

Disease of the ovaries is an important complication of this disease, and accompanies it with such frequency that some authors claim that it has some influence in its causation. Usually, it takes the form of excessive luteal development, especially in the formation of cysts, but it is difficult to determine the relation between the two conditions, as in many cases of chorio-epithelioma not even a corpus luteum is seen, and Seitz⁹ has proved that lutein elements are increased in every pregnancy. Experiments have even been carried out which seem to prove that the successful termination of a pregnancy depends upon this increase in the lutein tissue.

Pathological Anatomy.—Examination in situ with the naked eye shows the growth to be an irregular, diffuse, fungous mass deeply implanted in the uterine wall by numerous prolongations which run between the bundles of muscular fibres. At other times the surface is rough, ulcerated and coarsely ragged, with villous vegetations. At the seat of the disease, the uterine wall may be almost or entirely eaten through. Solivij¹⁰ reports a case where the disease had penetrated into the parametrium. More rarely, the growth may be pedunculated or the tumour may be sessile, nodules of it lying beneath the mucous membrane, which is apparently intact. The tumour varies considerably in size; it may

be as small as a marble, but almost never is larger than a foetal head at term. In colour, it is usually greyish, with dark hæmorrhagic spots, but it may be either dark green or bright red. The growth is usually soft and friable in consistence, never being firm as in fibroid disease, or hard, as is seen in ordinary epithelioma. It is usually situated high up near the fundus of the uterus, but the vagina may be the primary site and cases of this have been reported by Landau and Büsse. Landau's¹¹ patient was a girl of twenty, who had previously enjoyed the best of health. She was admitted to his clinic on November 9th, 1900, having been last "unwell" in the middle of the previous August. At the end of October, pain in the lower abdomen and bleeding came on. She was examined and the external os found to be closed. Curettage revealed nothing, but she suffered from repeated attacks of hæmoptysis. On November 9th, Landau found the uterus and ovaries to be healthy, but he discovered two swellings in the lower part of the left wall of the vagina near the introitus. One of these was the size of a bean, while the other was about twice as large. They looked like thrombosed veins and the mucosa over them was ulcerated, with blood at the base of the ulcer. No physical signs of pulmonary disease could be discovered. The vaginal masses were removed and the uterus curetted in February, 1902. Microscopic examination of sections of the nodules showed typical chorio-epithelioma, while the curettings presented nothing abnormal.

Contrary to most uterine growths, secondary deposits occur both early and frequently in chorio-epithelioma, and this fact may be considered as symptomatic of the disease. Extension takes place by means of the blood-vessels, and in many specimens one can see the tumour cells projecting into the blood-spaces or even lying loose there. A case reported by Lockyer, however, suggests their transmissibility through the lymphatics as well. The patient was 26 years old and had given birth to a full term child four weeks before coming under observation. Ten days after labour, she began to have dragging pains in the vagina accompanied by a brownish discharge, and ten days later a lump appeared in the groin. This mass did not show any glandular structure, but its appearance and situation were those of the inguinal lymphatics. The lungs are the organs which are the more prone to be affected secondarily, thus accounting for the cough, dyspnœa, hæmoptysis, etc., so often met with, and after the lungs comes the vagina. Here, the growth usually presents itself as a soft violet coloured nodule, which rapidly increases in volume, ulcerates and bleeds profusely. Kirman's statistics show 28 pulmonary to 20 vaginal metastases, while in my own series, there were 103 pulmou-

ary and 72 vaginal deposits. The nervous system may be affected as may also the bones, and none of the viscera have escaped.

Histology.—The typical elements of this tumour are (1) Small well-defined polyhedral cells with large vesicular nuclei packed together in masses without any connective tissue between them. (2) Large multi-nucleated masses of protoplasm (plasmodia or syncytia) in which no definite cell boundaries are visible. (3) Large cells, sometimes mono- and sometimes multi-nucleated, some of which resemble decidual cells, others being identical in character with the multi-nucleated giant-cells which occur in the decidua serotina. These in some parts are arranged in cell masses without intervening stroma, while in other places they are infiltrating and destroying adjacent tissues after the manner of sarcomata. The cells of the first class are those of Langhan's layer. When young, they are small, but they increase in size with age. Their nuclei contain a fine intra-nuclear network and are easily stained. They also contain glycogen. These cells of Langhan's constitute neither an important nor a necessary element in chorio-epithelioma and may be completely absent in undoubted cases of this disease. The same statement does not hold good, however, in regard to the syncytial masses, these being always present in these growths. The plasmodia or syncytia are not true cells, but are simply ill-defined masses of protoplasm with one or more nuclei. The protoplasm is usually homogenous and opaque and takes the staining reagents readily. The nuclei are small, oval or round, and are scattered throughout the mass without any semblance of order. They multiply by direct division and may be vacuolated. The syncytium forms the boundary of the growth, i.e., it is seen at the periphery. In the centre of the neoplasm, no vessels with true walls are seen, but the growth is nourished by lacunæ, the walls of which are composed of syncytial masses which penetrate the uterine wall. In doing so, they send long processes between the muscular bundles which run along the vessels and ultimately penetrate their walls. Before actually opening into the vessels, however, they cause a weakening of their walls, thus allowing of a localized dilatation of the vessel, which gives it an appearance of being thrombosed or varicose. After entering the vessel, these plasmodia actively proliferate and act in one of two ways. The mass in the vessel may form a thrombus, which may itself go to some distant part, or it may give off cells or smaller processes, which in their turn, travel with the blood stream and so give rise to new foci of disease. Or the thrombus may form and remain where it is, becoming canaliculized and taking the place of the vessel wall. The above process explains the manner of spread of the disease as well as the hæmorrhages which accompany it.

Haultain¹² thinks that many cases of cure may be explained by the blood being poured out around the neoplasm and cutting off its nourishment by pressure.

Marchand recognizes two forms of chorio-epithelioma, viz: the typical and atypical. The former is characterized by the presence of syncytial masses, sending off branches in various directions, thus forming a network, the strands of which are covered with nuclei and in whose meshes are clear cells which vary in number. In the atypical variety, the cells are irregular and compact, with very large deeply stained nuclei, and, while multinuclear cells are present there are no continuous plasmodial masses.

Symptoms.—Chorio-epithelioma may begin very insidiously by bringing out symptoms of some very different malady, as is seen in the case reported by Büsse.¹³ This patient had a fatal hemiplegia and the autopsy revealed the presence of chorio-epithelioma affecting the right Sylvian artery, with secondary deposits in the liver, spleen and right heart, the genitals being quite free from the disease, although the patient had suffered from a miscarriage six months previously. Usually, however, it is uterine hæmorrhage which first attracts attention. This bleeding is marked by its severity and its resistance to treatment, even curettage being of but very evanescent benefit. The blood loss rapidly impairs the patient's health; she loses weight and the skin becomes waxy. Between the hæmorrhages, there is a discharge which may be either serous, sero-sanguineous or smoky, and which has a foul odour. Local pain is either entirely absent until the later stages of the disease or else but slight. The patient may have chills, fever, vomiting, cough, purulent expectoration, hæmoptysis, nervous affections, etc., which are produced by the metastases, or in the case of the chills and fever by sepsis. Examination of the patient, where the uterus is the primary site of the disease, reveals that organ to be enlarged, but the amount of this enlargement varies, it rarely, however, being bigger than a foetal head at term. The surface may be either nodular or else smooth and even. Per vaginam, the cervix may be felt to be soft and the os, to be so patulous as to permit the entrance of the examining finger into the uterine cavity, where one may find a mass of soft, spongy material, resembling placental tissue. This growth is usually situated on the anterior or posterior wall of the uterus, near the top of the fundus. While exploring the cavity, the finger may remove a fragment of tissue for microscopic examination. Pigmentation of the skin, which is so often seen to accompany the usual forms of malignant disease, so far has not been recorded in chorio-epithelioma.

The duration of time which may elapse between pregnancy and the onset of the disease varies. Usually only two or three months intervene, but McCann reports a case with a nine years interval, Fleischman six years, and several with an interval of from two to three years. My own first patient afflicted by this disease had been delivered of a molar ovum three and a half years before showing any evidence of malignant trouble. There may, however, be no interval at all, the growth developing during the progress of a pregnancy.

Prognosis.—Generally speaking, echorio-epithelioma may be considered to be one of the most malignant tumours which attack the uterus. If not interfered with, death usually supervenes in a few weeks or months, but occasionally the patient may live for one or two years. If discovered early and treated radically, the patient may recover, and the same happy result has been reported even where no treatment was carried out; but in these cases the diagnosis has been doubtful. However, well authenticated cases have terminated favourably where only part of the growth was removed. In connection with this, a case reported by Dr. Charles V. P. Noble is of interest. In November of 1900, he removed a uterus for chorio-epithelioma. The bladder wall was also involved and the tumour implicating it was not touched, as its removal would have called for too extensive an operation. The patient made a good recovery from the operation and died of some rather acute pulmonary trouble in September of 1905. Dr. Noble saw her a few days before death and could then find no sign of any tumour or swelling in connection with the bladder or any other pelvic organ, so that it is strongly probable that the lung trouble was not consequent upon the former disease, as if any recurrence had taken place it would have been most likely to have done so in the bladder wall.

Velits considers¹⁴ that spontaneous cure may result from necrobiosis. "as shown by the lowered vitality and the disappearance of the cells of Langhan's, and the appearance of wandering cells which shows the separation of the syncytium." Cases similar to that of Noble; where the secondary nodules have not been touched, but hysterectomy has been performed and the patients have made permanent recoveries, have been reported by Albert, Kolomonkin, Marehand and others.

Those cases which follow moles are less virulent than those which are preceded by ordinary pregnancy, and, of the latter, those ending in abortion appear to have the highest rate of mortality. In my own series, the mortality was: after moles, 52.85 per cent.; after abortions, 63.75 per cent.; and after full term deliveries, 54.32 per cent.

There is nothing in the appearance of the elements of the tumour

which will help very materially in arriving at a decision regarding the ultimate fate of the patient, except that where you have a great number of the cells showing subdivision of the nuclei, you may expect a fatal result within a short time. The invasion of connective tissue by the epithelial cells has been thought by many to indicate malignancy, but Loeb¹⁵ has shown that in cases of transplantation of skin, epithelial cells were seen to be able to penetrate, not only connective tissue, but also even cartilage without being malignant. Velitz claims that the presence of wander-cells in the neighbourhood of chorio-epithelial growths is evidence of degeneration of the cells of that growth and so warrant a favourable prognosis, but Fleischman, Herman and Schmauch dispute this theory on the ground that it only applies to that group of cells which resemble puerperal wander-cells, and the distinction between these two groups of cells is not always easy.

The number of Langhan's cells in a tumour will be of some assistance, Schmauch saying that "the simple presence of Langhan's cells in larger numbers and their appearance in foci between muscle cells will always be sufficient to declare the case to be malignant." The atypical cases, composed of cells of the character of wander-cells and giant-cells without plasmodial masses have a favourable prognosis.

Diagnosis.—All cases of hæmorrhage from the uterus following pregnancy are not due to chorio-epithelioma, but in cases where it is severe and difficult to control, one should be suspicious, especially if the pregnancy has terminated in the discharge of an hydatid mole. It may be due to retention of products of conception, posterior displacements of the uterus, endometritis, inversion, carcinoma or some general systemic disturbance. The careful use of the curette with examination of the scrapings, will, however, usually clear up the diagnosis. Do not trust to the result of the curettage alone, as at least one case has been reported where it was found that the growth was distinctly pedunculated and the curette had gone all around it without touching it at all. Where curettage for hæmorrhage following pregnancy is followed by more blood-loss, especially if this is excessive, and cannot be controlled by either drugs or local treatment, where there is any foul discharge and cachexia, treat the case as one of chorio-epithelioma, and you will seldom be wrong. In fairness to our friends the pathologists, it is only just to say that it is extremely difficult to form any opinion as to the necessity or otherwise of operation by an examination of the scrapings, as, to be sure that removal of the uterus is necessary, you ought to find the malignant cells scattered through the muscular tissue, and, as a rule, none of this latter tissue is removed by the curette.

Treatment.—The treatment may be preventive, palliative or curative. The former consists in careful attention to the interior of the uterus after pregnancy, especially where this has terminated in an abortion. Before we knew how serious a condition might follow an expulsion of an apparently normal ovum, it was considered good treatment to leave an ovum, the subject of a "missed abortion," in the uterus for an indefinite time to see if it would not come away spontaneously. The same view regarding the treatment of a retained fragment of placenta was held by many. In the light of our present knowledge, however, I think that this line of treatment will be abandoned for one much more energetic and radical and that these foreign, and potentially dangerous bodies, will be removed with great care and thoroughness as soon as discovered, in order to prevent placental grafting with its possible serious results.

The palliative treatment is only to be adopted in cases where the growth cannot be removed. Tonics are indicated by the debility of the patient. The uterus should be everted, douched with an antiseptic solution and packed, and caustics or styptics may be applied to the interior of the uterus with benefit. All nodules in the vagina should be excised thoroughly and the incisions necessary for that purpose closed by suture. Pain and other complications are to be combated as indicated.

Where there is any chance of curing the patient, early and complete removal of the growth should be effected. If the uterus is the seat of the primary tumour, the whole organ should be excised, the appendages being removed with it, by either the vaginal or abdominal route as seems best to the operator. All enlarged glands are to be removed at the same time, even if they do not ultimately turn out to be infected by the growth, as it is impossible to determine this macroscopically.

The following are the reports of the cases which have occurred in Canada up to the present date:

1st. Writer's first case, reported in the *Montreal MEDICAL JOURNAL*, September, 1905.

Patient was 47 years of age and a unipara. Three and a half years before the onset of the symptoms of the present trouble, she was delivered of an hydatid mole. In June, 1904, she began to have an hæmorrhagic discharge from the vagina, and this has continued up to the time of her admission to hospital. At first, the discharge had no odour, but during the last few weeks it has been very disagreeable, and she has lost flesh. For the last five months she has been losing freely almost all of the time.

Until just before leaving for home after the operation, there was no sign of pulmonary involvement, but at that time she began to have a

cough. Nothing abnormal in the lungs could be made out on physical examination.

The examination of the genitals revealed a mass, ovoid in shape, attached by a comparatively narrow pedicle to the anterior vaginal wall and quite free from the uterus. It was about the size of a hen's egg, freely movable and of a greyish colour. The uterus was felt to be slightly enlarged and hard and its mobility was limited. To the left of the uterus could be felt a hard mass which was about the same size as that in the vagina.

The vaginal mass was removed under an anæsthetic and the uterus was curetted, but all of the diseased tissue could not be removed on account of its having extended deeply into the pelvis. The cavity was closed over by catgut sutures.

The patient went home, but died in about four months, fresh nodules of the disease having appeared in the vagina. The uterus also became considerably increased in size, evidently becoming the site of a metastatic growth. No autopsy could be obtained, so that one cannot speak with certainty as to the location of metastases; but as the patient suffered from cough before leaving hospital and a great deal of dyspnoea after arriving home, it is, at least, probable that there were secondary nodules in the lung.

Nothing abnormal was seen in the sections taken from the scrapings of the uterus, but those made from masses of the tumour of the vagina showed a new growth in the form of villi projecting into masses of degenerated tissue and blood, part of the latter being clotted and more or less organized. These villous-like processes contained numerous cells, closely packed together, with vacuolated nuclei; larger mono- or multi-nucleated cells, polygonal in shape; and, lastly, multi-nucleated masses of protoplasm without any cell-border.

2nd. Dr. Howitt, of Guelph, sent a uterus to Dr. John McCrae, for examination. (Case not reported).

Patient was 34 years old, had given birth to 10 full term children, and had suffered one miscarriage. Two weeks after the abortion, the woman began to have hæmorrhage from the uterus. It was profuse and did not yield to any kind of treatment. The uterus was felt to be somewhat enlarged and soft with a patulous os.

Complete hysterectomy was followed by death of the patient from "metastatic deposits in the lung." No autopsy was obtained.

Dr. McCrae has informed me that the uterus was enlarged to measure 11 x 6 x 9 cm., and that in the fundal region lay a rounded mass measuring 3 x 2 cm., firmly attached to the posterior wall about 2 cm. down

from the highest point of the cavity. This mass was whitish in colour, firm in consistence, and, when finally hardened artificially, broke away from the uterine wall, leaving a deep hollow. Sections of the growth showed that it was composed of Langhan's cells, large polygonal cells and syncytial masses, i.e., typical chorio-epithelial elements.

The next three cases were reported by Dr. M. J. Ahern, of Quebec, in the *Bulletin Médical de Québec*, July, 1907, and I am indebted to him for the notes.

3rd. Woman, aged 44 years, had given birth to eight full term children. She had four other pregnancies, one of which had ended in the discharge of an hydatid mole at the eighth month, this being followed by a severe hæmorrhage which was most difficult to control. Four months before admission to hospital, she had passed a second mole, this time at the second month of pregnancy. The lochia stopped on the eighth day, but two days later, she began to lose blood, which loss soon became very excessive. It was absolutely unaffected by treatment, even curettage being ineffectual. Uterus was enlarged and the os sufficiently dilated to admit the index finger. Two masses could be felt to be attached to the uterine wall, one being firm and the second soft and friable. Total hysterectomy was followed by recovery and the patient was well when the case was reported three years after operation.

On examining the interior of the uterus after removal, one small, glistening nodule was seen in the upper part of the posterior wall. To the left of this was a cavity filled with material resembling blood-clot, into which the finger could be easily forced. The adnexa presented nothing unusual. Microscopically, the invading masses were seen to consist of Langhan's cells and syncytium.

4th. Age 30. This woman had given birth to three full term children, one being born dead, and one pregnancy had ended in a miscarriage at the fourth month, in June, 1903. She continued to bleed until she entered hospital in the following July, and had suffered pelvic pain for some months. She was thin and pale, with an icteric tint in the skin and conjunctivæ. There had been cough and expectoration of blood for some time. There was a malodourous discharge from the uterus. The latter organ was felt to be enlarged, sensitive, and mobile. On the posterior vaginal wall were three bluish nodules, resembling hæmorrhoids. Curettage was attempted but had to be abandoned on account of hæmorrhage, and the patient died in a few days. No autopsy was obtained, but Dr. Ahern reports the diagnosis as "chorio-epithelioma with metastases in the vagina and lung."

5th. Age 19. Patient had given birth to two sets of twins. When the last were born, one was normal, but the other ovum had developed

into an hydatid mole. This delivery was followed by severe post-partum hæmorrhage. One month later, the woman began to lose blood, and this hæmorrhage resisted all kinds of treatment. When she entered hospital, the uterus was enlarged and the external os admitted the index finger with ease. Total abdominal hysterectomy was followed by recovery.

The adnexa were seen to be healthy. On cutting open the uterus, two friable nodules were seen on the wall. Sections of these showed a similar picture to that seen in case 4.

6th. Drs. Garrow and Keenan have at present under observation a case which is unique in Canada, and rare in any part of the world. It is one of chorio-epithelioma in the male. The patient is a young man, twenty years old, who bruised one of his testicles getting into a bath. This injury was followed by pain and swelling, for which Dr. Garrow removed the organ. Numerous metastases have appeared in the skin and sections from these and the original tumour show most typical chorio-epitheliomatous formation.

7th. Mrs. K., æt. 38, entered the gynæcological ward of the Montreal General Hospital on the 28th of May, 1907, with a history of having menstruated last on the third of the previous January. Sixteen days prior to admission, she had an attack of abdominal pain for two nights, followed by "flowing," and the blood loss had been continuous ever since. Three days before admission, she had severe cramp-like pains followed by an increase in the amount of the flow and the discharge of a "fleshy" mass, after which the pain and flow became less marked. Her menstrual history was negative and she had never been pregnant. The examination of the pelvic organs revealed a healthy vagina and a uterus which was slightly enlarged, the external os being patulous and cervix soft. An incomplete abortion was diagnosed and the uterus was curetted, examination of the tissue removed confirming the diagnosis. The operation was followed by a rather more profuse flow of blood than is ordinarily seen. She was readmitted on the 21st of November, 1907, complaining of "flooding." Since her return home, she had only been twice "unwell," viz: on July 3rd, and October 3rd, the flow being scanty each time. On November 14th, she began to have a foul smelling discharge from the uterus. This became blood stained the next day and has continued so ever since. On the 18th, the blood loss was very severe, going right through the mattress, and the next day she passed a mass which she said looked "like a bunch of veins." This was the size of a walnut. She has had one or two other hæmorrhages which were preceded by colicky pains. There has been loss of weight and strength.

Local examination, revealed a reddened area around the meatus, but the vagina was healthy. The cervix was firm and closed. The fundus

was in good position, mobile, firm, and the size of a two months' pregnancy. The appendages were not enlarged.

On account of the obstinate hæmorrhage, the passage of tissue resembling "a bunch of veins, the foul discharge and the loss of flesh, malignant disease, probably chorio-epithelioma, was diagnosed, and the uterus and appendages were removed." The patient made a good recovery, but before she left hospital, there was a small nodule to be felt in the vagina just below the cicatrix, and she had a cough. Dr. Finley examined the lungs and reported dulness over both bases posteriorly and the usual signs of the presence of fluid in the pleuræ. The pleural cavity was twice aspirated, but only a little bloody fluid found once.

On cutting open the uterus, it was found to measure 12.5 cm. in length with a wall 2 cm. thick. The cervix and lower part of the fundus appeared to be healthy, but in the fundus was a mass the size of a small hen's egg closely incorporated in the uterine wall. Projecting down from this was a ragged looking tongue of tissue 3.5 cm. in length. This whole mass looked bluish-red. A prolongation into the uterine end of the left broad ligament was seen.

Microscopic sections through this tissue showed it to be composed of muscle into which projected villous-shaped masses of cells, with evident signs of hæmorrhage. These cells were of three kinds. There were the numerous small rounded cells with vesicular nuclei, the cells of Langhan's, larger cells, polygonal in shape, some with single and some with multiple nuclei, and finally, numerous masses of syncytium. In places, small groups of these elements entirely surrounded by muscle could be seen, while elsewhere they appeared in large masses, and scattered throughout the field areas of blood and degenerated cells were evident.

The patient came back to hospital on the 16th of January last, on account of a profuse, foul vaginal discharge, and a sloughing mass 3 cm. in length by 1 cm. in breadth, was seen to involve the anterior vaginal wall, in the region of the nodule which was present when the woman last left the ward. This was curetted away and the edges of the wound so produced were brought together with catgut, union by first intention resulting, and the patient was discharged. She returned to the ward on March 30th, complaining of intense headache and vomiting. There had been a sudden attack of unconsciousness eight days previous. She remained in a comatose condition for some hours and seemed stupid when she recovered her senses. Her eye-sight had been failing for some time, so Dr. Mathewson kindly examined her eyes for me. He found "neurorinitis in both eyes with hæmorrhages, more marked in the right eye." The patient died quite suddenly on April 3rd.

At the autopsy, which was performed by Dr. Lyman, to whom I am indebted for a very complete report, numerous metastases were found. In the tissue between the bladder and vagina, was a mass of growth about 3.5 cm. in diameter, but the vaginal cicatrix was free from disease. Numerous small metastatic nodules were seen scattered throughout both lungs. The intestines were also studded with small masses of new growth. On examining the brain, the vessels were seen to be congested, and several nodules were noticed to be scattered through the lobes of the cerebellum and one in the right half of the cerebrum. Each of these nodules is dark and hæmorrhagic in appearance and is surrounded by an area of pigmentation.

In conclusion, I wish to thank Dr. Duval for much assistance, Dr. Fraser Gurd for the sketch of the uterus, and Mr. Wade for cutting and staining the sections which were under the microscopes.

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